Novel approaches to acoustic immunosensing of extracellular vesicles

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Extracellular vesicles (EVs) constitute a promising source of biomarkers for disease diagnostics and can be obtained via liquid biopsies from various bodily fluids. While much progress has been made in recent years, challenges remain on the sensitivity, specificity and clinical implementation of current analytical workflows.

Quartz crystal microbalance with dissipation monitoring (QCM-D) has lately emerged as a powerful alternative for the phenotypic detection of EVs, offering multiple modes of analyte discrimination by frequency and dissipation. In this talk, I will present recent activities in my group towards effective interfacing of QCM-D-based approaches for the immunosensing of EVs, including the use of additional electrochemical read-out via impedance spectroscopy (eQCM-D) and nanostructuring the biosensor surface to mirror lateral analyte feature sizes.

When comparing the various strategies, we found (A) a lowering of the detection limit by a factor of 2-4 when combining QCM-D in tandem with in-situ electrochemical impedance spectroscopy; (B) a higher degree of binding on nanostructured gold surfaces over flat surfaces, (C) a higher degree of binding when Au NPs on silica rather than on gold, and (D) a higher degree of binding when the nanostructured features were matched to the lateral dimensions of the EVs. Meanwhile, a clinically-relevant limit of detection of around 10^7 EV-sized particles / ml can be routinely achieved.

Crucially, this analytical platform provides novel opportunities to aid sensor development (e.g. when validating surface functionalization, biomarker recognition or calibrating alternative read-out mechanisms) as well as for quality control.

References:

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